Hepatoblastoma: Outcome of Management of Two Cases

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Abstract: Even though hepatoblastoma is the most common malignant hepatic tumour in children, it is still a rarely encountered childhood tumour. Survival outcome is better with the favorable histologic subtype. This report is focused on raising increase awareness of this rare tumour in our environment and also to report the outcome of management of two cases based on already established collaborative multicentre clinical trial studies.

The first case was a 6week old girl with a painless abdominal mass presenting in acute respiratory distress with severe anaemia. The serum level of AFP was ≥ 107,000ng/ml. Right tri segmentectomy was performed for excision of the pedunculated liver mass. Histology of the mass was consistent with hepatoblastoma with predominance of fetal components. Complete course of adjuvant cisplatin 3mg/kg mono therapy was administered.

The second case was a 7 year old, healthy looking girl presenting with a slow growing abdominal mass for 6 years. Her serum AFP level was ≥ 10,000ng/ml. At surgery an encapsulated huge gray looking tumour was found on the right lobe of the liver. An extended right hepatectomy was performed to remove the tumour. Histology revealed hepatoblastoma with teratoid components. Complete course of adjuvant chemotherapy made up of cisplatin 60/mg^{2}in combination with doxorubicin 30/mg^2 was administered.

Both patients did well and had uneventful follow-ups.

Keywords: Hepatoblastoma, Chemotherapy, Histology.

INTRODUCTION

Unlike nephroblastoma, hepatoblastoma is an uncommon paediatric embryonic tumour in our environment, [1] probably because of low survival rate of children from those recognized risk factors in our setting. Overall, it represents 1% of all paediatric tumours, and is by far the most common malignant hepatic tumour that occurs only in children [2]. Mesenchymal hamartoma, infantile haemangioendothelioma, undifferentiated embryonal sarcoma and rhabdomyosarcoma of the biliary tract are also other rare hepatic tumours found only in children. Hepatoblastoma primarily arises from the pluripotent stem cells of the liver of the embryo. Majority developed before 3 years of age, and has a distinct male preponderance, in a ratio 2:1 male-to-female [3].

The much report about improved survival outcome from hepatoblastoma have been primarily due to improved diagnosis and treatment according to protocols developed from large multicentre collaborative clinical trial studies [4-7].

This report is aim at raising awareness for such an unfamiliar tumour in our environment, also report the outcome of management of two cases in our setting as according to multicentre collaborative clinical trial studies.

CASE 1

A 6 week old girl the first set of twins delivered by a 19 years old house wife to a family of non consanguineous parents after 39 weeks of unsupervised pregnancy. She presented with abdominal distention, respiratory distress, constipation and vomiting for 4 days. Examination revealed an acutely ill child, dyspnaeic (respiratory rate 68 cycles/min) and dehydrated, pale (packed cell volume 25%), anicteric, afebrile (temperature 37.1^{0}C), heart rate 168 beats/min. Her weight was 3.65 kg, 73% of the expected. She had a right hypochondrial mass extending toward the epigastrium, which was hard and irregular. The mass measures about 8cm below the right sub costal margin. Rectum and other system examinations were unremarkable. The mass was shown arising on the right lobe of the liver, hyperechoic and measures 10.2 x 8.0 x 9.7cm on abdominal ultrasound scan. Intrahepatic bile ductules were not dilated. Liver function test, full blood count, and absolute platelet, clotting profile, electrolytes, urea and creatinine and viral screening were normal. Serum alpha-feto protein (AFP) level was ≥ 107,000ng/ml. After stabilization, the peritoneum was opened through a transverse supra umbilical incision. Intraoperatively, an encapsulated and pedunculated, huge grayish looking mass was found on the anterio-lateral surface

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of the liver (stage I) Children's Oncology Group (COG) clinical staging system, [8] Figure **1**. Right trisegmentectomy was performed using diathermy coagulation in combination with Pringles maneuver of the portal inflows to remove the mass. 150mls of fresh blood was transfused intra operatively. The peritoneum was closed over a sub hepatic drain, which was removed after three days. Histology revealed immature hepatocytic elements disposed in solid sheets, and nest devoid of mitotic cells with scanty neoplasm which were consistent with hepatoblastoma with predominant fetal component. Pre chemotherapy haematological parameters were unremarkable. She received 5 courses of three weekly adjuvant cisplatin (CDDP) 3mg/kg in 250mls of intravenous fluid slowly for 5 hours. She was transfused on two separate occasions during the course of the chemotherapy. The post chemotherapy serum alpha-feto protein was ≤ 20ng/ml. Her follow up had been uneventful.

CASE 2

A 7 year old girl, with a slow growing right hypochondrial swelling for 6yearduration, sometimes associated with dull aching non radiating pain. No any other compliant. She had uneventful pregnancy and

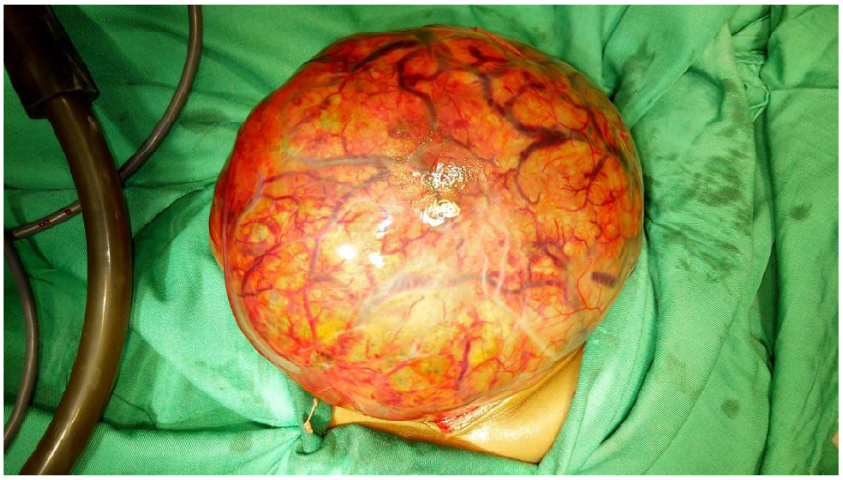

Figure 1a: Intra operative appearance of the liver mass in the 6 weeks old girl.

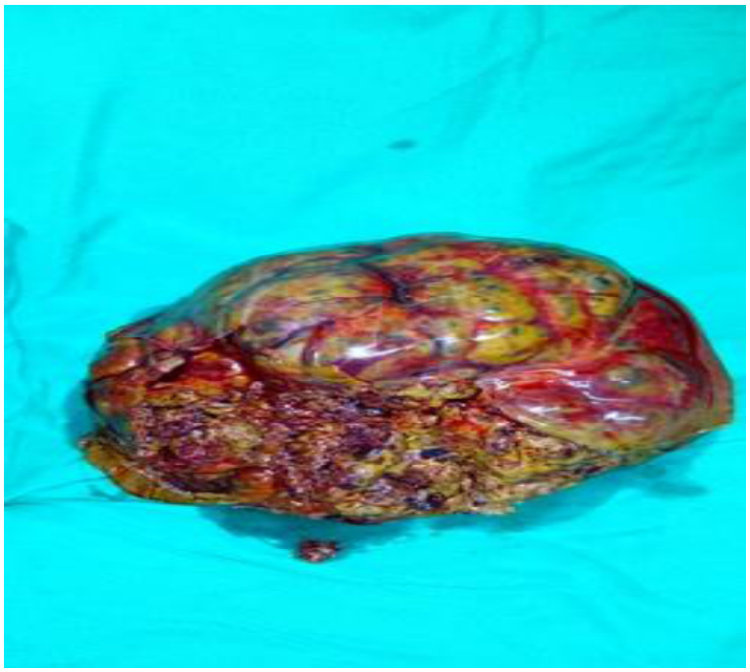

Figure 1b: Postoperative appearance of the mass after it was excised in a 6 weeks old girl.

delivery. The mother was 18 years old at the time of her birth. She was healthy looking on examination and weighed 19kg, 86% of the expected. Apart from a hard, non tender mass with irregular surface in the right hypochondrium extending toward the xphisternum, that measures 6cm below the right costal margin, otherwise abdomen was not distended. Other systemic examinations were normal. Her heamatological parameters and viral screening were normal. The serum level of AFP was ≥ 10,000ng/ml. Abdominal ultrasound showed a huge hyperechoic mass involving primarily the right lobe of liver measuring 15.7cm x 11.5 x 13.6 cm. Her chest X-ray was normal. A fine needle aspiration of the mass was suspicious of malignancy. The peritoneum was opened through a right subcostal hockey stick incision with a 3cm vertical extension toward the xphisternum. Intra operatively, a huge encapsulated grayish looking mass (stage I) COG Figure **2** involving the right lobe of the liver was found. An extended right hepatectomy was performed using diathermy coagulation combined with Pringles maneuver to remove the mass.500mls of blood was transfused intraoperatively. Grossly it weighed 560g. Histology of the mass showed liver tissues displaying fairly circumscribed malignant epithelial neoplasm, separated by fibrous bands forming nodular configurations with some focal areas showing differentiated chondroid and osteoid depositions, which were consistent with hepatoblastoma with teratoid features. Five courses 5 of three weekly combined adjuvant cisplatin 60mg/m^2 and doxorubicin 30mg/m^2 (PLADO) was administered. On completion of chemotherapy, the alpha-feto protein level dropped by more than 90% of its initial value. Her follow up had remained uneventful with regular (Figure **3**) abdominal ultrasound scan and alpha fetoprotein.

DISCUSSION

The aetiology of hepatoblastoma is still obscure, but has been associated with young maternal age < 20years, body mass index (BMI > 25), very low birth weight <1000g, perinatal oxygen therapy, treatment for infertility, and maternal substance abuse [9]. Certain genetic conditions such as: Beckwith-wiedemann syndrome, familial adematous polyposis, Gardner's syndrome, hemihypertrophy though not common but have been associated with hepatoblastoma [10, 11]. Young maternal age is the likely risk factor in our reports because both mothers were younger than 20 years.

The presentation in hepatoblastoma is almost similar to one of the most commonly diagnosed abdominal tumour in childhood in our environment. It presents as a painless abdominal mass, in an otherwise healthy looking child [12, 13]. Malaise, poor nutritional state from cancer cachexia will be obvious with advanced disease state. Jaundice is unlikely except when there is hilar obstruction by the tumour. At time there may be sudden intra tumoral or intra peritoneal haemorrhage leading to emergency presentation as seen in one of the patient that presented in acute respiratory distress with severe anaemia due to intra tumoral hemorrhage.

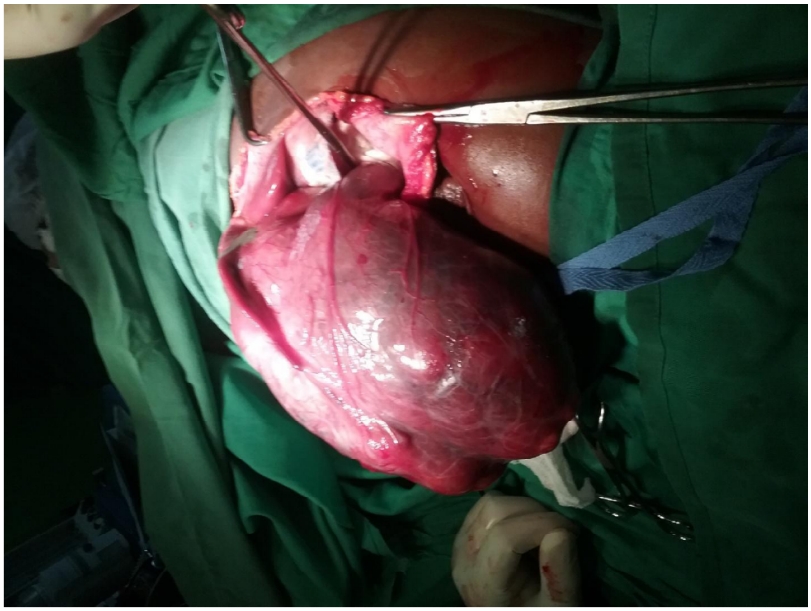

Figure 2a: Intra operative appearance of the right liver mass in the 7 year old girl.

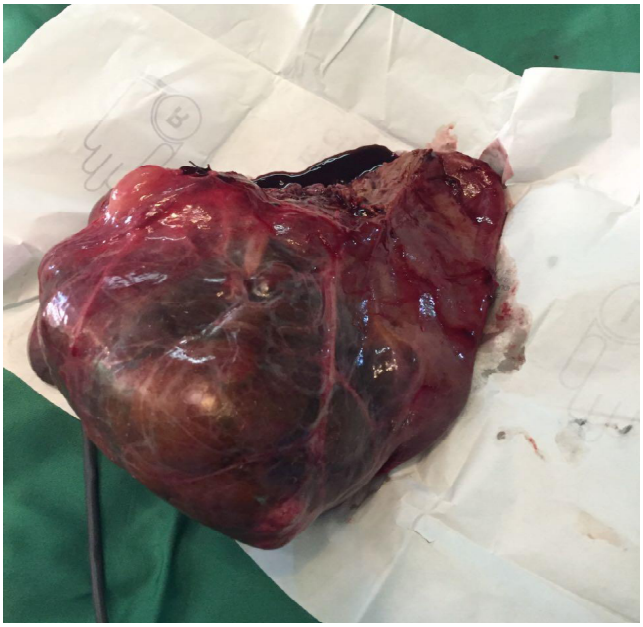

Figure 2a: The appearance of mass after it was excised in a 7 year old girl.

Occasionally there will be thrombocytosis because of excessive production of thrombopoietin by the tumour that can be picked on routine blood film [14].

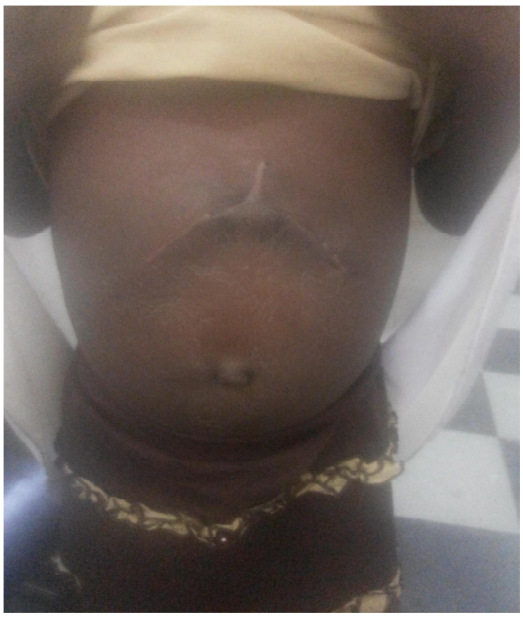

Figure 3: The 7 year old girl at her recent follow up 15 months after chemotherapy.

Ultrasound scan is the most common imaging tool for diagnosis of liver tomours, [15] however, when available computarised tomography scan (CT) or magnetic resonance imaging (MRI) gives superior definition of segmental involvement of the liver by the tumour in addition to tumour stage. Tumour echogenicty, dimension, and extension to the inferior vena cava and portal tract structures was determine with only abdominal ultra sound in this report.

The serum level of AFP was excessively elevated in both patients, even though other liver tumours such as hepatocelluar carcinoma, vascular tumours of the liver, harmatomas, adenomas and germ cell tumours, also produce AFP but not to such a very high level as with hepatoblastoma [16]. AFP is a protein predominantly produced by fetal yolk sac, liver hepatocytes and the gastrointestinal tract. Normal serum level of < 30ng/ml is often attained by 6 months to 1 year of life. Children with hepatoblastoma will have AFP level higher than normal for their age [17] Majority of children with hepatoblastoma will have an initial AFP level of between 100,000 and 1,000,000ng/ml especially the favorable histologic (pure fetal) subtype of hepatoblastoma [18]. Low levels of AFP < 100ng/ml is often encountered in small cell undifferentiated subtypes of hepatoblastoma, because of the decreased number of hepatocytes that secrete this protein in this subtype of hepatoblastoma which may suggest poor prognosis [19].

During the surgery, dissection of the liver tissue was performed with monopolar diathermy coagulation simultaneously with Pringle manoeuvre released after every 30minutes minimizing bleeding. The cut surface area was sutured over a cellulose polymer (surgicel) with an absorbable suture. The liver was not mobilized in the first patient because the tumour was pedunculated. Complete mobilization was done in the

second patient because of the size of the tumour which eased the resection.

Based on the histologic subtype and stage of the first patient, adjuvant cisplatin monotherapy was administered as according to reports, [20, 21] who confirm the efficacy of cisplatin monotherapy in stage I hepatoblastomas with favourable histology (fetal subtype), that completely resected. The histologic subtype of the second patient was unfavorable because of the presence of the teratiod features even though it was a completely resected stage I hepatoblastoma. Therefore received combined adjuvant chemotherapy PLADO.

The PRETEXT (pre treatment extent of disease based on radiologic location of the tumour) by the International Society of Paediatric Oncology (SIOP) and the clinical staging system by the COG are the most frequently used staging systems for hepatoblastoma [22]. The COG staging system is convenient for us because of our limited experience with this tumour and due to limlted availability of superior imaging studies such as CT scan and MRI in our own environment to stage the tumour before surgery.

Finally, the histologic characteristics of hepatoblastoma are important in streamlining overzealous exposure to the adverse effects of chemotherapy. A prognostically favorable histologic subtype, stage I, with serum AFP level > 10,000ng/ml like in the first case can receive a single chemotherapeutic agent as have been proven from multicentre clinical trial study groups [23].

Currently the two patients are doing well; the first patient is 18 months post chemotherapy, while the second patient is 15 months. Their follow is every 6 months with AFP assay.

In conclusion, hepatoblastoma is not a common tumour in our environment, however with proper planning and from experiences of previous studies its outcome is in no way different from the previous reports.

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